122. (Added) The method according to claim 121, wherein BMP-7 (OP-1) is about 200 ng/ml and parathyroid hormone is about 25-200 nM.

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REMARKS

THE CLAIM AMENDMENTS

Applicants have canceled claims 74-88, 90, 91, 95-99 and 103-105. Applicants have canceled these claims without prejudice and without waiver of their right to file for and obtain claims directed to any canceled subject matter in divisional and continuing applications which claim priority from this application.

Added claims 106-122 mimic claims 78-87 and 90-99 but recite methods of inducing local tissue formation rather than methods of treating a tissue degenerative condition. Support for added claims 106-122 is provided at specification pages 4, line 33-page 5, line 1; page 29, line 33-page 30, line 26; page 32, lines 4-18; and Figures 1, 7-9. None of these claims introduces any new matter.

As such, claims 69-73, 102 and 106-122 are pending in this application.

THE RESTRICTION REQUIREMENT

The Examiner has required restriction of the claims of this application under 35 U.S.C. § 121 into one of the following seventeen Groups:

Group I: Claims 69-73, 102 drawn to a method of inducing local tissue formation comprising implanting a morphogenic protein and IGF-I, classified in class 514, subclass 12;

Group II: Claims 74, 75, 103 drawn to a method of accelerating allograft repair and incorporation comprising implanting at a bone replacement locus a morphogenic protein and IGF-I, classified in class 514, subclass 12;

Group III: Claims 76, 104 drawn to a method of promoting integration of an implantable prosthetic device comprising administering a morphogenic protein and IGF-I, classified in class 514, subclass 12;

Group IV: Claims 77-88, 90, 91, 95-99, 102-105 drawn to a method of treating a tissue degenerative condition comprising administering a morphogenic protein and IGF-I, classified in class 514, subclass 12;

Group V: Claims 69-73, 102 drawn to a method of inducing local tissue formation comprising implanting a morphogenic protein and hydrocortisone, classified in class 514, subclass 179;

Group VI: Claims 74, 75, 103 drawn to a method of accelerating allograft repair and incorporation comprising implanting at a bone replacement locus a morphogenic protein and hydrocortisone, classified in class 514, subclass 179;

Group VII: Claims 76, 104 drawn to a method of promoting integration of an implantable prosthetic device comprising administering a morphogenic protein and hydrocortisone, classified in class 514, subclass 179;

Group VIII: Claims 77-88, 90, 91, 95-99, 102-105 drawn to a method of treating a tissue degenerative condition comprising administering a morphogenic protein and hydrocortisone, classified in class 514, subclass 179;

Group IX: Claims 69-73, 102 drawn to a method of inducing local tissue formation comprising implanting a morphogenic protein and insulin, classified in class 514, subclass 4;

Group X: Claims 74, 75, 103 drawn to a method of accelerating allograft repair and incorporation comprising implanting at a bone replacement locus a morphogenic protein and insulin, classified in class 514, subclass 4;

Group XI: Claims 76, 104 drawn to a method of promoting integration of an implantable prosthetic device comprising administering a morphogenic protein and insulin, classified in class 514, subclass 4;

Group XII: Claims 77-88, 90, 91, 95-99, 102-105 drawn to a method of treating a tissue degenerative condition comprising a morphogenic protein and insulin, classified in class 514, subclass 4;

Group XIII: Claims 69-73, 102 drawn to a method of inducing local tissue formation comprising implanting a morphogenic protein and PTH, classified in class 424, subclass 198.1;

Group XIV: Claims 74, 75, 103 drawn to a method of

accelerating allograft repair and incorporation comprising implanting at a bone replacement locus a morphogenic protein and PTH, classified in class 424, subclass 198.1;

Group XV: Claims 76, 104 drawn to a method of promoting integration of an implantable prosthetic device comprising administering a morphogenic protein and PTH, classified in class 424, subclass 198.1;

Group XVI: Claims 77-88, 90, 91, 95-99, 102-105 drawn to a method of treating a tissue degenerative condition comprising administering a morphogenic protein and PTH, classified in class 424, subclass 198.1;

Group XVII: Claim 88 drawn to a method of treating a tissue degenerative condition comprising administering a morphogenic protein and an indeterminate agent that increases IGF-I bioactivity, indeterminate class and subclass.

The Examiner contends that the inventions encompassed by Groups I-XVII are patentably distinct from one another and have acquired a separate status in the art. The Examiner contends that the following pairwise combinations of methods are independent and distinct, wherein each member of a pair performs different functions, using different starting materials and/or process steps: I and each of II-XVII; II and each of III-XVII; III and each of IV-XVII; IV and each of V-XVII; V and each of VI-XVII; VI and each of VII-XVII; VII and

each of VIII-XVII; VIII and each of IX-XVII; IX and each of X-XVII; X and each of XI-XVII; XI and each of XII-XVII; XII and each of XIII-XVII; XIII and each of XIV-XVII; XIV and each of XV-XVII; XV and each of XVI-XVII; XVI and XVII. Applicants traverse this restriction on the basis of the procedures set forth in the Manual of Patent Examining Procedure ("MPEP").

The MPEP states that if the members of a Markush group are sufficiently few in number that a search and examination of the entire claim can be made without serious burden, "the examiner must examine all members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions" (emphasis added). MPEP §803.02. Applicants respectfully request that the Examiner reconsider the restriction requirement in view of this MPEP procedural rule.

Applicants respectfully request that Groups I, V, IX and XIII be examined together. Each of those Groups recites a method of inducing local tissue formation comprising implanting a morphogenic protein and a different MPSF. The MPSFs, IGF-I, hydrocortisone, insulin and parathyroid hormone in claims 69-73, 102 and 106-122 are recited as members of a Markush group. This Markush group is made up of only four members. Four members is "sufficiently few" and accordingly, the Examiner must examine all four members together.

If the Examiner does not agree with applicants' proposal to rejoin Groups I, V, IX and XIII, applicants provisionally elect with traverse the claims of Group I

(claims 69-73, 102) for initial substantive examination. 37 C.F.R. § 1.143. This election is made expressly without waiver of applicants' rights to continue to prosecute and to obtain claims to the non-elected and/or canceled subject matter either in this application or in other applications claiming priority herefrom.

ELECTION REQUIREMENT

The Examiner has also required that applicants, pursuant to 35 U.S.C. § 121, elect a single disclosed species from:

(a) jaw bone locus
(b) bone defect locus
(c) bone replacement locus
(d) joint locus
(e) nervous system-associated tissue locus

The Examiner further states that claims 69-73, 102, 76, 104, 77-88, 90, 91, 95-99, 102-105 are generic and that the reply to the species election must include a listing of all claims readable thereon.

Applicants elect the species bone defect locus. Claims 69, 71, 102 and 106-122 read on the elected species bone defect locus.

The Examiner further states that if the species bone defect locus is elected, then applicants must further elect a single disclosed species from:

(a) fracture
(b) non-union fracture
(c) fusion
(d) bony void

The Examiner further states that claim 71 is generic and that the reply to the species election must include a listing of all claims readable thereon.

Applicants elect the species fracture. Claims 69, 71, 102 and 106-122 read on the elected species fracture.

The Examiner has also required that applicants, pursuant to 35 U.S.C. § 121 elect a single disclosed species from:

(a) a homodimer comprising at least one BMP-2 subunit
(b) a heterodimer comprising at least one BMP-2 subunit
(c) a homodimer comprising at least one OP-1 subunit
(d) a heterodimer comprising at least one OP-1 subunit
(e) BMP-2 polypeptide
(f) BMP-4 polypeptide
(g) BMP-5 polypeptide
(h) BMP-6 polypeptide
(i) BMP-7 polypeptide
(j) BMP-8 polypeptide
(k) BMP-9 polypeptide
(l) BMP-10 polypeptide
(m) BMP-11 polypeptide
(n) BMP-12 polypeptide
(o) BMP-13 polypeptide
(p) COP-5 polypeptide
(q) COP-7 polypeptide

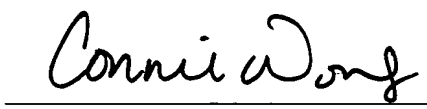
The Examiner further states that claims 69-88, 90, 91, 95-99 and 102-105 are generic and that the reply to the species election must include a listing of all claims readable thereon.

Applicants elect the species BMP-7 polypeptide. Claims 69-73, 102 and 106-122 read on the elected species BMP-7 polypeptide.

CONCLUSION

In view of the above, applicants request that the Examiner examine the pending claims in this application. Applicants request favorable consideration and early allowance of the pending claims.

Respectfully submitted,



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Appendix of Amendments

106. (Added) The method according to claim 67, wherein the morphogenic protein comprises a pair of subunits disulfide bonded to produce a dimeric species and wherein at least one of the subunits comprises a polypeptide belonging to the BMP protein family.

107. (Added) The method according to claim 67, wherein the morphogenic protein is an osteogenic protein.

108. (Added) The method according to claim 107, wherein the osteogenic protein is capable of inducing the progenitor cell to form endochondral or intramembranous bone.

109. (Added) The method according to claim 107, wherein the osteogenic protein is capable of inducing the progenitor cell to form cartilage.

110. (Added) The method according to claim 69, wherein the morphogenic protein is capable of inducing the progenitor cell to form tissue tendon/ligament-like or neural-like tissue.

111. (Added) The method according to claim 69, wherein the morphogenic protein comprises a polypeptide selected from the group consisting of: BMP-2, BMP-4, BMP-5, BMP-6, BMP-7 (OP-1), BMP-8, BMP-9, BMP-10, BMP-11, BMP-12, and BMP-13, COP-5, COP-7.

112. (Added) The method according to claim 69, wherein the morphogenic protein comprises a polypeptide selected from the group consisting of BMP-7 (OP-1), BMP-2, BMP-4 and BMP-6.

113. (Added) The method according to claim 69, wherein the morphogenic protein comprises BMP-7 (OP-1).

114. (Added) The method according to claim 106, wherein the dimeric species is a homo- or hetero-dimer comprising at least one BMP-2 or BMP-7 (OP-1) subunit.

115. (Added) The method according to claim 69, wherein the morphogenic protein stimulatory factor is IGF-I.

116. (Added) The method according to claim 69, wherein the morphogenic protein is present in the pharmaceutical composition at a concentration of at least about 1 ng/ml, and the morphogenic protein stimulatory factor is present in the pharmaceutical composition at a concentration of at least about 0.01 ng/ml.

117. (Added) The method according to claim 69, wherein the morphogenic protein is BMP-7 (OP-1) and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is IGF-I and is present in the pharmaceutical composition at a concentration of from about 0.1 ng/ml to about 50 ng/ml.

118. (Added) The method according to claim 69, wherein the morphogenic protein is BMP-7 (OP-1) and is

present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is hydrocortisone and is present in the pharmaceutical composition at a concentration of from about 0.05 nM to about 5.0 nM.

119. (Added) The method according to claim 118, wherein BMP-7 (OP-1) is about 200 ng/ml and hydrocortisone is about 0.5 - 5.0 nM.

120. (Added) The method according to claim 69, wherein the morphogenic protein is BMP-7 (OP-1) and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is insulin and is present in the pharmaceutical composition at a concentration of from about 0.01 nM to about 1000 nM.

121. (Added) The method according to claim 69, wherein the morphogenic protein is BMP-7 (OP-1) and is present in the pharmaceutical composition at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor is parathyroid hormone and is present in the pharmaceutical composition at a concentration of from about 10 nM to about 1000 nM.

122. (Added) The method according to claim 121, wherein BMP-7 (OP-1) is about 200 ng/ml and parathyroid hormone is about 25-200 nM.